Third. Actual lesion of the sympathetic system, while far more common than heretofore supposed, is not necessary to produce the varied symptomatic phenomena of the disease. Functional disorder, through irritation conveyed from the adrenals, may sometimes cause all the symptoms—just as in chorea and in many of the conditions of aggravated hysteria, and other functional nervous disorders, we are often unable to find definite lesions.

Fourth. In a certain proportion of cases (not over 20 per cent.) the adrenals are affected by some other lesions than those of tuberculosis, or else they remain normal (in 12 per cent.) and the sympathetic nerves and ganglia are alone diseased.

I am aware that the objection may be raised that excessive pigmentation and even more extensive alterations are not infrequently found in the sympathetic ganglia, giving rise to no symptoms whatever (as in Case XXVI. above reported), and also that there is a tendency of late among physiologists to assign less independence and less functional importance to the sympathetic nerve system. In Addison's disease there are but three reasonable hypotheses to account for the symptoms, namely, that it is a blood disease; that it is due to adrenal toxins; or, that it is due to sympathetic irritation, either functional or organic. The latter hypothesis, while perhaps not wholly satisfactory, appears to be supported by much weightier evidence than either of the others.

While these views are not new (*vide* Greenhow "On Addison's Disease," Croonian Lectures for 1875), by many they have not been finally adopted, because experimental and statistical data have been very slowly accumulated; and it has been my aim, by experiment and by analysis of all recorded cases, to place on a somewhat firmer basis the belief that Addison's disease is dependent upon lesion or irritation of the abdominal sympathetic nervous system.

THE BACILLUS PYOCYANEUS PERICARDITIDIS.[1]

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Much attention has been given of late years to the effects of the cultures, and their products, of Gessard's B. pyocyaneus, especially in anthrax. At various times authors have announced the isolation of bacteria very closely resembling this, but the only one that seems to have gained a permanent place in literature is the B. pyocyaneus β of

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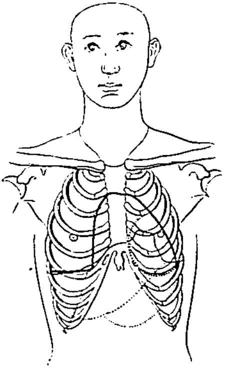
[1] Presented at the annual meeting of the Association of American Physicians, May, 1893.

P. Ernst, described by him a number of years ago. The differences, as given, are not marked, and Gessard is not inclined to acknowledge that they are due to more than temporary conditions, which appears the more justifiable, for the reason that these differences are largely simple variations in degree and intensity of color-production. It is not only upon differences in degree of color-production that the separation of the organism described in this paper depends, but upon differences of size as well, and the position taken appears to be justifiable because these differences have been found to be constant through a long series of cultures and controls.

The material from which the bacillus was originally obtained was placed in my hands by Drs. Councilman and Whitney, and came from a case in the service of Dr. F. C. Shattuck (at the Massachusetts General Hospital—"having been sent into the house from my service in the O. P. D."), to whose courtesy I am indebted for the following notes from the records.

October 26, 1892. J. E. H., aged forty-seven years, male, laborer, Demerara. No family history. Denies venereal disease. Pneumonia eight years ago. Malaria three years ago, with no periodicity. Signs of effusion about the heart, as per diagram, showing dull area to right of sternum and included in heavy black line. To the right of the sternum was heard a to-and-fro friction murmur, high pitched and well marked. Respiratory murmur not heard over the dull area. Fibrillary twitching of the left pectoralis major. Cardiac sounds more and more muffled as the apex was approached.



Oct. 27, 1892. Line of effusion. Systolic murmur within broken lines.

November 18. Examination of lungs absolutely negative. Some cough at night with no expectoration.

19th. Pericardium tapped in fifth interspace just inside the line of flatness. About three-quarters of a quart removed and sent to Dr. Whitney for examination. Reasons for tapping: 1st. Increasing and disproportionate rapidity of respiration as compared with the pulse and temperature curves. 2d. Increasing loss of flesh and strength. 3d. Non-absorption of fluid in pericardium. 4th. Sudden attack of weak heart and embarrassed respiration.

26th. Tapped again. Some of fluid sent to Dr. Councilman, who reports plenty of tubercle bacilli and a new bacillus which liquefies gelatin.

December 17. Tapped a third time; one quart and one gill removed.

March 5. Tapped in sixth space half an inch outside of nipple, and a pint of yellow turbid fluid obtained.

12th. Eloped (and could not be traced).

As will be seen from these brief extracts, the case is one of extreme interest from a clinical point of view. It will be reported at length by Dr. Shattuck in connection with others. The part of it that should be spoken of here concerns only the gross appearances of the fluid removed at the various tappings, and the micro-organisms it contained.

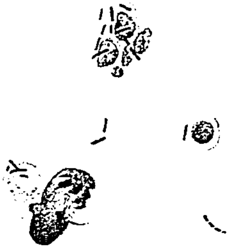
The results of the last tapping I did not see. Those of November 26th and December 17th were a fluid, clear and amber-colored, faintly alkaline, and depositing a slight sediment only after standing. There was no odor, but a very large per cent. of albumin, the fluid coagulating very readily by heat, and when sterilized forming an apparently very favorable medium for the development of the bacillus found in it.

The microscopic examination by Dr. Councilman showed a number of the bacilli of tuberculosis and a second bacillus whose arrangement *in the cells* of the fluid attracted his attention, because of its unusual character. (See Plate.)

At my request a portion of the fluid was given to me for bacteriological analysis. Plate cultures in gelatin, and needle cultures in blood serum showed the presence of no other organism than one corresponding in its appearance, under the microscope, to that seen in the original fluid. Such an examination was made a second time of the fluid removed upon December 17th, with the same results. From these cultures, a long series of tests have been made upon a large number of different media, and under different conditions of temperature.

Every step in the investigation has been checked by and compared with cultures of the bacillus pyocyaneus derived from the following sources:

1. My own laboratory culture, which came originally from the Hygienic Institute, in Berlin, and has been under constant cultivation.
2. The laboratory of Johns Hopkins University; sent to me by Dr. Welch, he being not quite certain of the origin of the culture.



Cover-glass preparation of pericardial fluid, stained by the Koch-Ehrlich method. The red rods are bacilli of tuberculosis. The blue rods are the bacillus pyocyaneus pericarditidis. (Comp. oc. 12. Apochrom. obj. 1.30. Camera lucida.)

3. The laboratory of the College of Physicians and Surgeons; sent to me by Dr. Cheesman, at Dr. Prudden's request, and coming originally from Prague.

4. The Army Medical Museum; given to me by Dr. Gray, and of uncertain origin.

Inasmuch as cultures from all these sources substantially agreed in gross appearances and under the microscope, minor variations in rapidity of growth and intensity of color-production being left out of account (for these were more in one at one time and in another at another), and at the same time, inasmuch as they all differed in the same way and under the same conditions from this new bacillus, the conclusion is irresistible that the organism is in reality an undescribed variety, and differs from the bacillus pyocyaneus by well-marked and constant characteristics. The results of the culture experiments have been tabulated for convenience sake, and the description of the B. pyocyaneus of Gessard and the B. pyocyaneus β of P. Ernst are added for ease of comparison. These are the only two organisms with which this B. pyocyaneus pericarditidis is in the least likely to be confounded.

BACILLUS PYOCYANEUS PERICARDITIDIS.

ORIGIN. Pericardial fluid, containing also bacilli of tuberculosis.

FORM AND ARRANGEMENT. Small straight bacilli, with rounded ends, three or four times as long as broad, and on most media slightly larger than the B. pyocyaneus of Gessard, occurring within the cells in the original fluid, and sometimes showing two or three end to end, but never observed in long chains.

MOTILITY. Actively motile in hanging-drop culture. No cilia or flagella have been demonstrated.

GROWTH. *Gelatin: Plates.*—Colonies appear at the end of 36–48 hours, as fine white points in interior, and upon the surface of the medium; edges are sharply defined; soon there appears a circular zone of liquefaction, finally passing through the stratum of the medium with the colony at the bottom. Under a low power the centre of the colony may be of a brownish color. On the second day a greenish tinge may be seen about the individual colonies on the surface which spreads through the entire medium. The plates may always be distinguished from those of the B. pyocyaneus of Gessard by the *bluish-green* when contrasted with the yellowish-green color of this latter.

Gelatin: Needle cultures.—At end of 24 hours a small saucer-shaped depression of liquefaction at upper end of needle track, which gradually spreads and deepens until the liquefaction extends straight across the tube and about half-way down the needle track. A bluish-green fluorescence appears about the liquefied portion at the very upper part of the gelatin, later changing into a yellowish-green. The colony is deposited as a yellowish heavy,sediment at the bottom of the liquefied portion, the upper part of which is clear. A small whitish growth occurs along the remainder of the needle track. Old cultures, in which a certain amount of evaporation has occurred, assume a very dark greenish-black color.

Agar-agar.—Along the needle track appears a *flat*, dry colony of a dirty grayish-white color spreading out upon each side of the needle track and growing, at first, upon the surface of the water of condensation, later depositing a white sediment at the bottom. From the first there may be detected, by reflected light, a metallic lustre on the surface of the colony in places, which metallic sheen later spreads over the whole colony and furnishes a marked differentiating point. In addition to this, within 24–48 hours at 37° C., there appears a green fluorescence throughout the whole of the medium, which increases slowly to a marked *bluish-green* color, and never assumes the nut-brown of the B. pyocyaneus of Gessard upon the same medium. The colony is not especially viscid.

Potato.—There appears a reddish-brown colony along the needle track, elevated and moist, confined to the line of the needle. Presents no change of color upon touching with needle, but certain specimens (as do some of the B. pyocyaneus) develop later a heavy green color extending over the whole surface of the potato, which later changes almost to black.

Bouillon.—Twenty-four hours at 37° C. gives a growth, especially on the surface, which is a wrinkled scum; no cloudiness of the bouillon, and a very faint greenish fluorescence .1 cm. below surface. At this time differs from the B. pyocyaneus of Gessard, in that the latter shows cloudiness of the medium all through. Later the same cloudiness appears in bouillon cultures of this new bacillus, together with a whitish sediment deposited at the bottom of the tube, and then the cultures are indistinguishable from each other. Same changes, but slower, occur at room temperature.

Peptone.—1, 3.5, and 6 per cent. solution. Twenty-four hours at 37° C. gives faint bluish tinge at upper edge of medium with very faint cloudiness; later (in one to two weeks) there forms a marked scum upon surface that is difficult to break up by shaking, and the whole medium assumes a grass-green color of more or less intensity and not seen on other similar bacilli. The shape and size of the organism, under the microscope, differs very markedly in this medium from any other bacilli examined. Same changes to be seen at room temperature, but more slowly.

Egg-Albumin: Plain.—Twenty-four hours at 37° C., yellowish-white, very profuse growth all along the needle track; yellowish-green spreading out from it almost to sides of tube, and in the condensation water as well. The growth has no especial distinguishing characteristics. Irregular liquefaction occurs, but the growth at no time differs in any marked way from other varieties of the B. pyocyaneus.

Blood-serum.—Twenty-four hours at 37° C. shows flat, moist colony with bluish-green fluorescence in its neighborhood. Liquefaction begins early and goes on slowly until complete in from one to two weeks, with an increasing intensity of color which becomes markedly blue, and eventually almost black.

Milk.—Behaves as do the other bacteria.

BEHAVIOR TO TEMPERATURE. Grows at 15–25° C., slowly; much more freely at 35–38° C., when it produces the color more quickly.

RAPIDITY OF GROWTH. Moderate.

SPORE-PRODUCTION. Not observed.

NEED OF AIR. Does not grow under mica. Facultatively anaërobic, but does not produce color except with free access of oxygen.

GAS-PRODUCTION. Produces faint foul odor.

BEHAVIOR TO GELATIN. Liquefies gelatin slowly.

COLOR-PRODUCTION. Produces a bluish-green color which in old cultures changes almost to a black. Upon the addition of acids (both vegetable and mineral) to cultures the color changes to red, and upon the addition of alkalies a bright grass-green appears. This reaction is best seen in bouillon and gelatin cultures, but occurs in other media as well, notably blood-serum.

BEHAVIOR TO ANILINE DYES. Stains easily and well with any of the aniline dyes usually employed, and by Gram's method.

MICROSCOPIC APPEARANCES IN DIFFERENT MEDIA. Under the microscope its general appearance on various media is of a rod larger than the B. pyocyaneus. In peptone cultures this difference is very marked. In this case, the B. pyocyaneus tested appeared as very short oval bacilli, almost like micrococci, while the new bacillus showed as a long fine rod, from four to six times as long as broad, about one-half the diameter of a red blood-corpuscle, and arranged sometimes two or three end to end. These same cultures transferred to gelatin became indistinguishable from each other in size.

Pathogenesis. Injections of small quantities (0.5 cm.) of a bouillon culture twenty-four hours old into the abdominal cavity of rabbits and guinea-pigs, killed 50 per cent. in from twenty-four to thirty-six hours. Autopsy showed general congestion of abdominal viscera, slight effusion into the peritoneal cavity, and cover-glass preparations and cultures showed the bacilli in the effusion in the abdominal cavity, as well as in the blood from the heart and various organs.

BACILLUS PYOCYANEUS. (GESSARD.)

Origin. In "green" pus. Really the green color only appears after exposure to oxygen, so that the pus itself is never green as a result of growth of the organism.

Shape and Arrangement. Short fine rods; often can be confounded with cocci.

Motility. Actively motile.

Growth. *Gelatin: Plates.*—After two or three days the entire plate has taken on a clear green color (grass-green), the surface colonies liquefying the gelatin in a funnel shape. Under a low power the deeper colonies appear round and somewhat yellowish, with clear, strongly refracting granular edges.

Needle cultures.—After twenty-four hours the upper surface of the gelatin is liquefied in a funnel-shaped depression with fluorescent coloring (grass-green) of the upper surface. The liquefaction later extends straight across above the solid portion to the sides of the tube, and the whole gelatin takes on a beautiful fluorescence.

Agar-agar.—Moist greenish-white layer along the needle track and spreading out on each side, and the whole agar becomes colored with a diffuse, beautiful fluorescence (grass-green), which later turns to a nut-brown color.

Potato.—Dry nut-brown elevated colony along the needle track. With ammonia it takes on a green, with acids a red color.

Milk.—Produces a yellowish-gray layer at upper part; produces casein, and peptonizes it ~~with help~~ of ammonia.

Behavior to Temperature. Grows well at summer temperature.

Rapidity of Growth. Grows rapidly.

Spore-production. Not observed.

Need of Air. Will not grow under mica plates.

Gas-production. Not observed.

Behavior to Gelatin. Liquefying.

Behavior to Aniline Dyes. Produces blue pigment, pyocyanin. Stains easily with ordinary aniline dyes and by Gram.

Pathogenesis. Guinea-pigs inoculated in abdominal cavity are killed (Koch). Rabbits inoculated in blood-current live.

BACILLUS PYOCYANEUS β. (P. ERNST.)

Zeit. f. Hyg., Bd. ii. S. 36, ii.

Origin. In the pus of gray-colored dressings.

Form and Arrangement. Small, very slender rods, not producing chains, but only two or three together at the most, probably possessed of cilia.

Motility. Actively motile.

Growth. *Gelatin: Plates.*—Colonies never sharply defined, but with delicate radiating threads, which are always visible, until by liquefying in circular form the colony sinks to the bottom in an irregular mass. The neighboring portion of the medium is colored green.

Needle cultures.—In the shape of, at first, a round and soon a pointed, deeply widening champagne-glass shaped liquefaction with a slowly appearing green coloring of the medium.

Agar-agar.—As a greenish-white but dry layer along needle track, with green coloring of the agar.

Potato.—From a fawn to nut-brown dry colony, which turns gray when touched with the platinum needle. The "chameleon" phenomenon. Different from B. pyocyaneus *a*.

Bouillon.—A thin spider's-web-like growth on surface, which, by shaking, easily collects into skeins and sinks with difficulty. The upper part of the bouillon is colored green.

Milk.—Green color at upper surface; rapid coagulation and energetic peptonizing of the casein.

BEHAVIOR TO TEMPERATURE. Grows at 15–25° C., but luxuriantly at 35–40° C., when it produces the green color more quickly.

RAPIDITY OF GROWTH. Grows with moderate rapidity.

SPORE-PRODUCTION. Not observed.

NEED OF AIR. Strongly aërobic.

BEHAVIOR TO GELATIN. Gelatin is rapidly liquefied and turned into a fluid as thin as water.

COLOR-PRODUCTION. Produces a yellowish-brown color, which very easily changes by oxidation into a dark-green. It is sufficient to shake the cultures, thus bringing in the oxygen of the air, to produce a dark-gray color. Old cultures turn a strong black-brown.

PATHOGENESIS. Not known.

SUMMARY.

The essential differences between this organism and those with which it has been possible to compare it are therefore as follows:

I. *Macroscopic.* 1. The bluish-green tinge of the gelatin in plate culture, as seen by reflected light, as distinguished from the yellowish-green tinge of the others.

2. The dryness and metallic lustre of fresh colonies and the bluish-green color, by reflected light, of old cultures upon agar-agar, as distinguished from the moist elevated fresh colonies, and nut-brown color, by reflected light, of old colonies of the others.

3. The greenish color of the colonies in peptone solutions of varying strength as distinguished from the bluish color of the other bacteria tested with it.

4. The very much greater rapidity and intensity of the reaction of gelatin and bouillon cultures to acids (red color) and alkalies (grass-green).

II. *Microscopic.* The variations in its appearance under the microscope.

1. From gelatin, indistinguishable.

2. From peptone, long, slender rods, as contrasted with short oval ones,

3. On other nutrient media, its general average as a larger rod, which can be made out by comparative examination, but is hardly subject to measurement. It can be seen, however, in preparations from egg-albumin, bouillon, blood-serum and potato. Only upon gelatin and agar is there no appreciable difference.

It appears, therefore, justifiable to conclude that we are dealing with a distinct variety of the bacillus pyocyaneus, and that Gessard's conclusion that there is but one is unfounded.